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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

F16

Office Action Summary	Application No. 09/634,320	Applicant(s) Papisov
	Examiner Jane Zara	Art Unit 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 7, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above, claim(s) *1-13, 18, 23-27, 31-33, 35, and 38-96* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *14-17, 19-22, 28-30, 34, 36, and 37* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *15, 18*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed April 7, 2003, Paper No. 17.

Claims 1-96 are pending in the instant application.

Election/Restriction

This application contains claims 1-13, 18, 23-27, 31-33, 35 and 38-96 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's election with traverse of nucleic acid and polyacetal carriers, and intercalators as the drug in Paper No.13 is acknowledged. The traversal is on the ground(s) that appropriate reasons have not been established for the restriction of the different and distinct compositions of Group II, which compositions contain a multitude of components, comprising: (single stranded or double stranded) nucleic acid drug carriers; polysaccharide, polyacetal, polyether polymers, oligopeptides, oligosaccharides or a specific combination of polymers or oligomers; and a nucleic acid, polypeptide or chemical drug. This is not found persuasive because drug carriers comprising either single stranded or double stranded drug carriers in combination with (covalently attached or reversibly associated) polysaccharides, polyacetals, polyethers, oligopeptides or oligosaccharides; and nucleic acids, polypeptides or chemical drugs including intercalators, are chemically, biologically, structurally and functionally distinct from each other and thus one does not render

oligopeptides or oligosaccharides of the drug carrier complexes and vice versa, and the nucleic acid drug components are not necessary to make the polypeptide or other drug components of the drug carrier complexes, and vice versa. Furthermore, the subject matter and field of art required to properly search one group of compounds or compositions is not coextensive or significantly overlapping with the very diverse subject matter required to properly examine the other compounds or compositions. Searching the appropriate art for all of the diverse multitude of compounds and compositions claimed would indeed be a serious burden to the examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13, 18, 23-27, 31-33, 35 and 38-96 have been withdrawn from further consideration. Claims 14-17, 19-22, 28-30, 34, 36 and 37 have been examined on their merits as indicated in the Office action set forth below.

Response to Arguments and Amendments

Any rejections not repeated in this Office action are hereby withdrawn.

Applicant's arguments with respect to claims 14-17, 20-22, 28-30 and 34 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14-16, 20-22, 34, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Warren.

Warren (document "**AN**", provided in IDS, Paper No. 18, filed April 7, 2002) teaches drug carriers comprising a nucleotide with less than 5% moisture content by weight, and further comprising a drug component, and which drug carrier component optionally further comprises a biocompatible polymer, which nucleotide drug carrier component is either double or single stranded, and which polymer is optionally covalently linked (or crosslinked) to the nucleotide, and which polymer optionally comprises two (chemically distinct) polymeric components and has an aqueous solubility of at least 1 mg/liter at 25°C, and which drug for delivery optionally comprises a nucleic acid or non-nucleic acid component (See abstract; page 9, line 11-page 14, line 18; page 16, line 29-page 20, line 2; figures 1-26; page 26, line 19-page 28, line 5; page 32, line 5- page 33, line 24; claims 1-4, 10-13 and 22-28.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-17, 20-22, 28-30, 34, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warren as applied to claims 14-16, 20-22, 34, 36 and 37 above, and further in view of the combination of Matysiak et al, Ishihara et al, Gao et al and Burke et al.

The claims are drawn to drug carrier compositions comprising a nucleotide component, a biocompatible polyacetal polymer component and a drug which comprises an intercalating agent, wherein the polymer and the nucleic acid components are optionally covalently crosslinked, or wherein the polymer, drug and nucleic acid components are reversibly associated, and which polymer component has an aqueous solubility of at least 1 mg/liter at 25°C.

Warren is relied upon as cited in the 102 rejection above.

Warren does not teach drug carrier compositions comprising intercalating agents, nor comprising polyacetal polymers, nor comprising optionally reversibly associated drug, non-drug nucleic acid and polymeric components.

Matysiak et al teaches bioconjugates comprising covalent conjugation or crosslinking of oligonucleotides to other molecules utilizing acetal moieties and derivatives thereof, and which

polymer component has an aqueous solubility of at least one mg/liter at 25°C (see entire document, especially figures 2 and 3 on pages 856-857, and the text on pages 857-860).

Ishihara et al teaches drug carriers comprising nucleotide components and intercalating agents, which are optionally covalently conjugated or alternatively linked via reversible associations, including ionic complexes (see especially col. 1, lines 24-55).

Gao et al teaches the use of intercalating agents as anticancer drugs, whereby the bis intercalating agent, ditercalinium, induced DNA repair in target cells (See especially 2422 and first paragraph of the discussion on bottom of page 2424- top of page 2425).

Burke et al teach diagnostic, therapeutic or prophylactic drug carrier compositions comprising a biocompatible, polyacetal polymeric component, and comprising double stranded or single stranded polynuceotides, and which polymer component is optionally heterogenous or homogenous (i.e. optionally comprising at least two chemically distinct polymers), which drug carrier complex comprises reversible associations (i.e. salt or ionic bridges, hydrogen bonding) between the polymer, nucleic acid and drug components (See entire document, especially col. 2, line 44- col. 5, line 11; col. 6, line 64- col. 7, line 16; claims 3 and 11).

It would have been obvious to one of ordinary skill in the art to design and utilize drug carriers comprising a nucleotide component and a biocompatible polyacetal component because drug carriers comprising nucleic acids and non-nucleic acid drugs, and optionally comprising polymers have been taught previously by Warren, and drug carrier complexes have been successfully designed and utilized for the target cell delivery of various agents including for labile

drug delivery, as taught previously by Burke et al. One of ordinary skill in the art would have expected that nucleic acid components are used for cellular delivery of both nucleic acid and non-nucleic acid drug delivery because such drug carriers have been taught previously by Warren. One of ordinary skill in the art would have been motivated to utilize such drug carriers for target cell delivery of therapeutic or diagnostic agents because these biocompatible complexes have been shown by Burke et al to enhance delivery of labile drugs to target cells upon administration to an organism compared to drugs administered without protective carrier complexes, providing increased quantities of drugs to the target cell in a biologically active form. One of ordinary skill in the art would have expected that biologically compatible nucleotide conjugates are obtained utilizing acetal containing polymers because nucleotide conjugation to various moieties utilizing acetal groups have been taught previously by Matysiak et al, and covalently linked nucleotide drug carrier conjugates have been shown to have enhanced biological stability in appropriate biological contexts compared to non-conjugated drug carriers, as taught previously by Warren and Ishihara et al. One of ordinary skill in the art would have been motivated to utilize polyacetals in generating nucleotide containing bioconjugates or drug carriers because conjugates containing varying stoichiometries of conjugate components are generated utilizing polyacetal groups, allowing flexibility to optimize for best stoichiometries for a particular drug carrier complex in order to achieve a desired biological effect. One of ordinary skill in the art would have been motivated to utilize intercalating agents for therapeutic or diagnostic purposes because intercalating agents are known to be successfully delivered to target cells as bioconjugates, as

taught previously by Ishihara et al, where the intercalators insert themselves into double stranded DNA, and intercalating agents have been used historically to generate mutations in the DNA of target cells or alternatively for detection or diagnostic purposes, once delivered to a target cell. In addition, the bis-intercalating agent, ditercalinium has been used as an anticancer drug by inducing DNA repair systems when delivered to target cells, as taught previously by Gao et al.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

KAREN LACOURCIERE
PATENT EXAMINER

JZ

June 19, 2003